Introduction

Vascular anomalies are commonly diagnosed in infants, children, and young adults, representing a vast array of disorders ranging from simple birthmarks like naevus simplex or “stork birth” to life-threatening, multisystemic malformations.1 Complex, systemic variations can be difficult to diagnose due to variable phenotype presentations and overlapping symptoms, ultimately causing patients to present to numerous subspecialties searching for answers. While some vascular anomalies can be classified as tumors or malformations, kaposiform hemangioendothelioma (KHE) has components of both.

This is a complex case of a young girl with an unusual presentation that ultimately required the dedication of multiple subspecialties to reach a rare diagnosis.

Case Summary

A 12-year-old female patient presented in March 2018 with a large epidural hematoma after sustaining a low-velocity injury from a dog bite requiring an emergent craniotomy. However, the degree of bleeding for the location and level of impact was noted as unusual. At the time, she was found to be mildly thrombocytopenic and mildly coagulopathic. Testing for an oncologic origin of the thrombocytopenia and coagulopathy was pursued from then on. She met criteria for coagulopathy and was identified to have a mutation in COAGA gene leading to Hypoaglobulinemia Translocase (HBT) which were negative. She was discharged with outpatient follow up.

In early 2019, the patient was readmitted for suspected bacterial meningitis, and she was again found to have mild coagulopathy with thrombocytopenia and a serum d-dimer. Upon follow up MRI, brain and spine, there was concern for an underlying systemic process due to bone marrow involvement, lymphadenopathy, pulmonary fibrotic changes. Blunting of bilateral optic disc with increased complexity of bilateral optic nerve sheath fluid was also noted, and patient was started on acetaminophen, while all complaints of chronic headaches improved. Due to these findings, she was transferred to the hematologist oncologist, dermatologist, and ophthalmologist, as well as a lymph node biopsy (via EUS) showed fibrotic proliferation. A bone marrow biopsy (performed at time of evaluation) showed the setting of a neoplastic process (possible lymph node), which was concerning for gross masses. Masses were comprised of thickly and thinly walled vascular spaces (some communicating) with flat endothelium. Pathology, these findings are typically observed in cases of cavernous hemangiomas, although not enough specimen was obtained for further staining or genetic sequencing.

The patient completed the radiation treatment follow up with multiple subspecialties, all the while remaining asymptomatic aside from occasional headaches, and persistent thrombocytopenia and coagulopathy. Her case was reviewed in the UTHealth Vascular Anomalies Clinic and in conjunction with her subspecialists, it was decided that she should undergo repeat chest imaging with MRI to better visualize her mediastinal mass (image 3), followed by bronchoscopy and laryngoscopy biopsy given the persistent pulmonary fibrotic changes seen throughout her course. These studies ultimately contributed to a full evaluation and ended up leading to a final diagnosis of kaposiform hemangioendothelioma.

Table 1: Summary of patient’s findings by subspecialty

The patient continued her radiation treatment follow up with multiple subspecialties, all the while remaining asymptomatic aside from occasional headaches, and persistent thrombocytopenia and coagulopathy. Her case was reviewed in the UTHealth Vascular Anomalies Clinic and in conjunction with her subspecialists, it was decided that she should undergo repeat chest imaging with MRI to better visualize her mediastinal mass (image 3), followed by bronchoscopy and laryngoscopy biopsy given the persistent pulmonary fibrotic changes seen throughout her course. These studies ultimately contributed to a full evaluation and ended up leading to a final diagnosis of kaposiform hemangioendothelioma.

Discussion

KLA is a commonly described vascular anomaly that is associated with a high mortality rate. Malformations and tumors are found throughout the body in multiple organ systems (such as the musculoskeletal), bone, and viscera. Serious complications that can be seen include severe lymphedema, hearing loss, and multi-systemic organ failure. Patients with KLA typically present with respiratory involvement including symptoms of cough or dyspnea, along with bleeding concerns such as hematuria, due to the lymphorrhagic, hemorrhagic, or inflammatory disease with worsening respiratory symptoms and hemorrhage. Outcomes in a hallmark for KLA and mortality is most associated with cardio-respiratory failure.2 KLA is frequently diagnosed based on pathology, which has characteristic clumps or sheets of small pulmonallymphatic endothelial cells accompanied malnourished lymphatic channels.3

Diagnosing KLA can be a challenge and often is created from multiple specialists to reach a diagnosis due to its multisystem involvement. As seen in Table 1, the range of positive exam findings throughout our patient’s journey encompassed multiple organ systems. The patient’s thrombocytopenia and coagulopathy were noted and evaluated at the time of her initial presentation and has been the highest risk complication for her throughout her journey given the developmental delay, and previously noted hemorrhagic concern.

The MRI imaging of our patient’s chest (images 3 and 4) show her pulmonary vascular dilatation, thinning, diffuse pulmonary interstitial thickening and pleural effusion.

Unfortunately, KLA has a poor prognosis with a 5-year survival rate of 75% and a median survival rate of 489 months.4 However, there has been some success in the use of sirolimus or Rapamune, an mTOR inhibitor, to control survival and management, as well as possible treatments for brain aneurysm and/or fistulae for treatment. Studies on KLA cells have shown inappropriate activation of the PI3K/AKT/mTOR pathway (figure 1), specifically AKT and MAPK activator, therefore, inhibiting mTOR disrupts proliferation and overgrowth. A 2016 study published on Sirolimus in KLA patients where all patients with continued treatment showed no disease progression.5 Our study included patients with KLA and showed similar findings, in which some patients have been shown to normalization of platelet levels and coagulopathy. The mechanism of action is not clearly understood, but potentially functions. However, it is important to be aware of the possibility of disease symptoms tailoring after discontinuing treatment.

Conclusion

Although kaposiform hemangioendothelioma is rare, it is important to know the clinical presentation, the diagnosis, and the treatment. As in the case presented here, the patient presented with symptoms that may raise a patient presents with multisystem involvement and possible vascular anomaly. In terms of treatment, advancements in genetics and knowledge of cell proliferation pathways allow for new and better treatments, such as utilization of mTOR inhibitors. More awareness of vascular anomalies specifically KLA is a critical diagnosis and therefore earlier treatment, hopefully leading to more successful outcomes.

References


Texas Pediatric Society Electronic Poster Contest